Amselem disclose solid dry coprecipate compositions containing lipophilic active ingredients comelted with tocopherol polyethyleneglycol succinate (TPGS) and a dispersion adjuvant. Amselem describes that conventional lipophilic substances were usually administered in the form of liquid preparations. However, the bioavailability of the formulation is very low. (See col. 1, lines 29-37). Accordingly, Amselem provided a solid composition for improved bioavailability.

In contrast to the invention defined by the present claims, Amselem does not teach or suggest a fluid pharmaceutical composition comprising an aqueous dispersion of micelles in which the micelles comprise a podophyllotoxin. Instead, Amselem teaches a solid composition of a lipophilic substance and TPGS. There is no teaching or suggestion in Amselem that a liquid form of the Anselem composition could be used. To the contrary, Amselem teaches away from the use of a liquid form by teaching a liquid form has low bioavailability. Further, even if the solid Amselem composition was converted to a liquid in the body there is no teaching or suggestion that a micelle would be formed comprising podophyllotoxin.

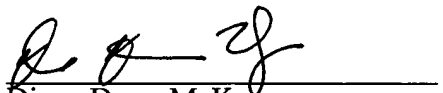
In addition, Amselem does not disclose or suggest that an aqueous dispersion is formed of micelles having an average diameter of less than about 300 nm. Applicants have surprisingly found that biological agents can be delivered to target tissue such as small capillaries while protecting uptake by non-target tissues by using a predetermined size of micelles. (See, page 25, line 29-page 26, line 20 of the application.) Further, it has been demonstrated that species with micelles greater than about 300 nm are ineffective for cell transfection. In contrast, there is no teaching or suggestion in Amselem that selection of the claimed size of micelles comprising podophyllotoxin could have advantages. Further, one of ordinary skill in the art would not look to Amselem for realizing the advantages for a micelle particle size of less than about 300 nm for delivering a podophyllotoxin. Further still, Amselem does not teach or suggest a method of treating an animal by administering a fluid pharmaceutical composition comprising an aqueous dispersion of micelles comprising podophyllotoxin having an average diameter of less than about 300 nm. Also, Amselem does not teach or suggest a method of delivering a podophyllotoxin of etoposide and teniposide by administering a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm. Accordingly, the invention defined by the present claims is not obvious in view of Amselem.

Accordingly, Brandely et al. do not cure the deficiencies of Amselem noted above. Further, there is no motivation for one skilled in the art to combine Amselem directed to a solid composition with Brandely et al. directed to a intravenous injection and even if the references were combined the invention is not obvious since neither reference teaches a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm, the micelles comprising a podophyllotoxin of eptoside or teniposide and a surfactant.

In view of the foregoing, Applicant submits that all pending claims are in condition for allowance and requests that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. A fee in the amount of $110 for a one-month extension of time is enclosed. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

In the event the fee tendered herewith is deemed inadequate, authority is hereby given to charge any such deficiency or credit any overpayment to Deposit Account No. 13-2165 Mathews, Collins, Shepherd & Gould. The Examiner is invited to contact the undersigned if further information is required.

Respectfully submitted,



Diane Dunn McKay
Reg. No. 34,586
Attorney for Applicants

DATE: December 5, 2001

MATHEWS, COLLINS, SHEPHERD & GOULD, P.A.
100 Thanet Circle, Suite 306
Princeton, New Jersey 08540-3662
Telephone: (609) 924-8555
Telecopier: (609) 924-3036